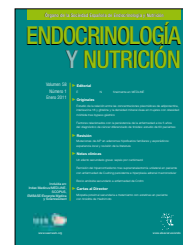


ENDOCRINOLOGÍA Y NUTRICIÓN

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SCIENTIFIC LETTERS

Height and weight development in an adolescent with complete growth hormone deficiency secondary to a craniopharyngioma

Desarrollo estatura-ponderal en un adolescente con déficit completo de hormona de crecimiento secundario a craneofaringioma

Growth from the fetal stage to adult age is conditioned both by determinant factors (genetic endowment) and regulatory factors represented by growth hormone (GH), insulin-like growth factor type 1 (IGF-1), thyroxine, insulin, sex hormones, and by environmental factors including nutrition, intercurrent diseases, and socioeconomic factors. All of these factors determine the final height of an individual, but GH is crucial for normal linear growth from the end of the first six months of life. At puberty, sex hormones stimulate GH amplitude and pulsatility and the local action of IGF-1 on growth cartilage. Thyroxine is needed for GH secretion and stimulates IGF-1 synthesis and action upon cartilage.

Insulin has a promoting action of mitogenic growth mediated by IGF-1 and other growth factors. The biological effects of insulin and IGF-1 are mediated by two different but structurally related receptors expressed in the cell membrane and belonging to the tyrosine kinase receptor family. A comparison of the amino acid sequences of insulin and IGF-1 (IGF-IR) shows an 84% identity in the tyrosine kinase domain and a 44% identity in the carboxyl end. Insulin has a 500 times greater affinity for its receptor than IGF-IR¹.

GH deficiency becomes clinically apparent as growth arrest and low height, together with decreased bone age and growth velocity.

Craniopharyngioma is a tumor with a benign histological behavior arising from the Rathke pouch. It is uncommon and accounts for 2%-5% of intrasellar or suprasellar primary intracranial tumors. The tumor most commonly occurs from 5 to 14 years of age. Its clinical presentation is due to anterior tumor expansion leading to visual involvement as its most relevant sign, or to posterior expansion causing hypothalamic involvement. The tumor is associated with obesity and hyperphagia in 39% of patients. Special mention should be made of the prevalence of panhypopituitarism before or after tumor surgery². GH deficiency occurs in 67%-

90% of patients before surgery, and in 73%-95% after surgery². Growth is therefore compromised in most patients^{3,4}, who show different responses to GH replacement therapy.

We report the case of a 7-year-old boy who was diagnosed with a suprasellar craniopharyngioma and treated by three-stage surgery for tumor recurrence and subsequent external radiotherapy on the residual tumor. After this treatment, panhypopituitarism was diagnosed, requiring replacement therapy with thyroxine (150 µg/day), hydrocortisone (20 mg/day), and inhaled desmopressin (20 µg/day). At subsequent visits, treatment was shown to have achieved good clinical and biochemical control.

After surgery, a complete deficit of the GH-IGF-1 axis was found, as shown by GH levels < 0.05 ng/mL, IGF-I levels < 25 ng/mL, and IGF-1 binding protein-3 (IGFBP-3) levels of 1.5 µg/mL. Similar values were found at four subsequent measurements. Prolactin levels were normal, and insulin levels (ranging from 41 and 98 mU/mL) in the presence of normoglycemia confirmed the existence of hyperinsulinism. The target height calculated based on family height was 166.5 cm (father's height 165 cm, mother's height 155 cm). The height of the boy was first measured at 7 years, following diagnosis of craniopharyngioma. Figure 1 and Figure 2 show height development and growth velocity tables. These show, after growth arrest following surgery, a constant growth rate which accelerated when androgen therapy was started at the chronological age of 16.5 years. Gonadotropins were first given to promote puberty, testosterone gel (50 mg/day) was subsequently used, and testosterone cypionate 10 mg/21 days was prescribed at the final assessment for hypogonadism, cryptorchidism, and immaturity of the scrotal sac. In the final visit at a chronological age of 18.5 years, the patient was at stage 2 of the Tanner development scale and had a bone age of 16 years. Patient weight was at all times above p > 97.

Despite the total absence of GH and IGF-1, this patient experienced, after the initial arrest attributable to surgery, sustained growth above the target height, with a markedly delayed bone age. He showed obesity and normoglycemic hyperinsulinism, together with a marked increase in growth velocity after the start of testosterone treatment. Accelerated closure of epiphyseal cartilages had not occurred at the time of writing. Although the mechanism inducing growth in the absence of GH and IGF-1 is unknown, cases reported in the literature suggest that hyperinsulinism

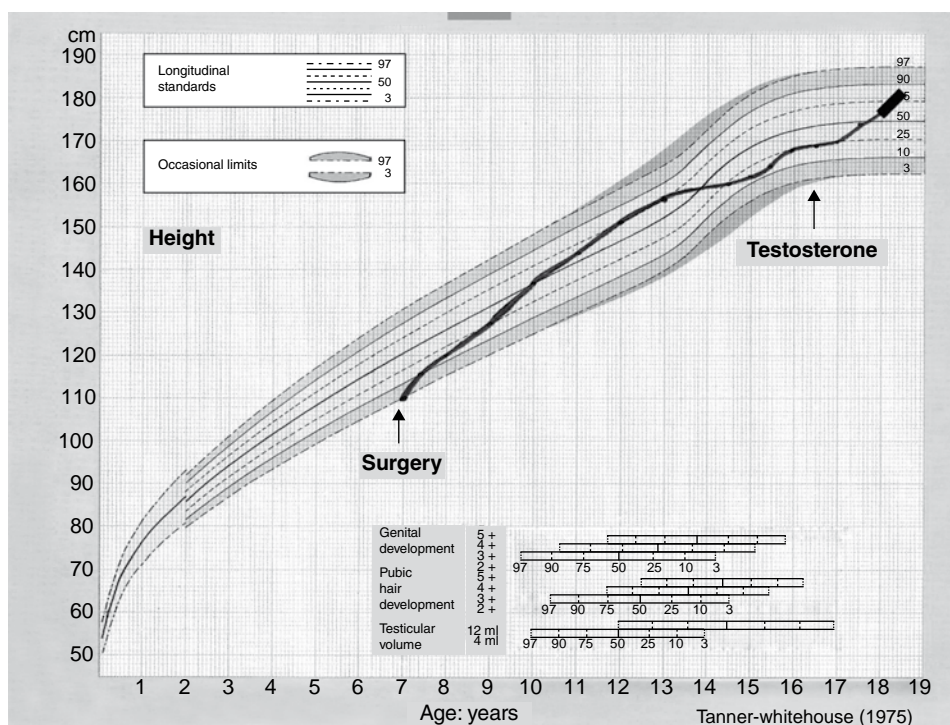


Figure 1 Height chart of the reported patient over time. Arrows indicate the time of surgery and start of testosterone treatment.

associated with obesity could explain IGF-IR stimulus in these patients. The initial description⁵ of a group of children with craniopharyngioma subject to surgery reported sustained growth only in the group with obesity, hyperphagia, hyperinsulinism, and hyperprolactinemia. The action

mechanism that sustains growth in these patients is unknown. Hyperprolactinemia⁶, leptin⁷, and above all insulin have been suggested as potential ligands of IGF-IR in growth cartilage. This action would be enhanced by the sex hormones.

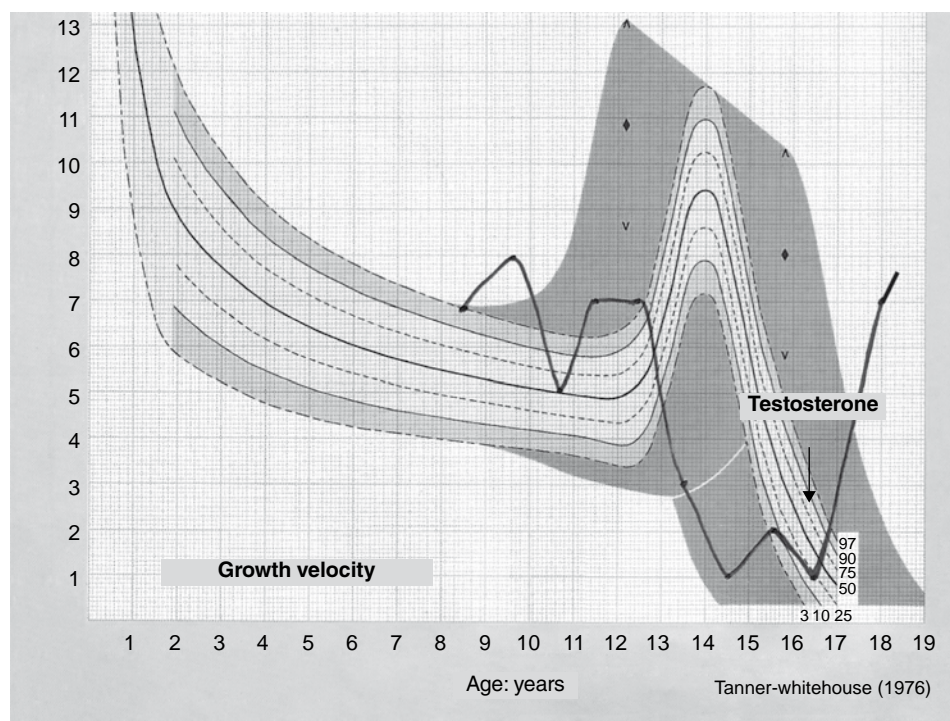


Figure 2 Growth velocity chart of the reported patient over time. Arrow indicates the start of testosterone treatment.

The Tiupalkov² study reported a follow-up of 25 patients who underwent surgery for craniopharyngioma, and found a correlation between the height appropriate for bone age and the body mass index of patients. Hyperinsulinism was seen in one third of the patients, almost all of whom had suprasellar tumor expansion and hyperphagia. These findings agree with those reported by Di Batista et al⁸, who found normal growth in eight out of 32 patients despite GH deficiency. Obesity, hyperphagia, and hyperinsulinism were also found in most of them.

Patients with panhypopituitarism after surgery for teratoma⁹ and congenital panhypopituitarism¹⁰ associated with normal growth and hyperinsulinism have been reported.

Clinical presentation of this case and a review of the literature on the subject suggest a significant effect of hyperinsulinism on IGF-IR, a promoter of longitudinal growth. This suggests the need for reflection and the conduct of large observational studies, minimizing bias, at a time when the role of insulin and its analogues on cell proliferation is being questioned.

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Follicular thyroid cancer presenting as radiculopathy. Ten years of follow-up

Radiculopatía como forma de presentación de un carcinoma folicular de tiroides. Evolución a 10 años

Differentiated thyroid carcinoma (DTC) is the most common endocrine cancer. An increased incidence of this tumor, both real and resulting from improved diagnostic techniques, has been reported in recent decades^{1,2}. Distant metastatic disease occurs in 5%-15% of patients³ and usually consists of asymptomatic pulmonary lesions. DTC diagnosis based on

symptoms of metastases is exceptional^{4,5}. However, an atypical presentation is seen in some cases, such as the one reported below.

In 1999 a 54-year-old woman attended the orthopedic surgery clinic reporting radicular pain over the previous year along with loss of strength in the left lower limb and constitutional symptoms. Lumbosacral magnetic resonance imaging (MRI) showed an expansive mass in the left hemisacrum, the biopsy of which was consistent with the metastasis of a follicular differentiated thyroid carcinoma. Examination revealed a mass on the right side of the neck. Tumor mass was completely resected by total thyroidectomy and resection of a grossly involved tracheal fragment. A histopathological study revealed a 4 x 3 x 2.5 cm follicular